

# THE ASSOCIATION BETWEEN DIETARY FACTOR OF LOW LEVEL MAGNESIUM AND DEVELOPMENT OF PRE-ECLAMPSIA AND ECLAMPSIA

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**Abstract:** All consenting 300 cases of normal level of serum magnesium pregnant women and 300 women with low level of serum magnesium attending antenatal clinic for antenatal checkup of  $\geq 20$  weeks who fulfills the inclusion and exclusion criteria were included in the study. Each patient were included only once in the study. Gestational age, parity, socioeconomic status and BMI were matched between cases and controls. History noted and after general physical and obstetric examinations, urine analysis is done to note the extent of proteinuria by dipstick method or by 24 hours urine protein estimation. Then 4 ml of venous blood is drawn from the subjects and sample is analysed for magnesium. Serum magnesium was measured by Calmagite method. Result: Of the 300 cases of low serum magnesium level primigravida pregnant women, 24 developed pre-eclampsia and 2 developed eclampsia. The subjects were primigravida in the age group of 18-30 years and belonging from low socio-economic status. The mean serum magnesium was  $1.137 \pm 0.280$  in the cases of low level of serum magnesium. In contrast out of 300 cases of normal level of serum magnesium primigravida pregnant women, 6 developed pre-eclampsia. The subjects were primigravida in the age group of 18-30 years and belonging from low socio-economic status. The mean serum magnesium was  $1.921 \pm 0.322$  in the cases of normal level of serum magnesium. The difference between the mean serum magnesium level in low level of serum magnesium cases and normal level of serum magnesium cases was statistically significant ( $p=0.0018$ ).

**Keywords:** Eclampsia, pre-eclampsia, proteinuria, serum magnesium.

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## I. INTRODUCTION

### BACKGROUND:

Hypertension is one of the most frequently encountered medical disorder in obstetrics practice and remain a major cause of maternal, fetal and neonatal morbidity and mortality. The present study was undertaken to compare the maternal serum magnesium levels in pre-eclampsia, eclampsia and in normal pregnant women.

Hypertension in pregnancy is an universal problem complicating 10% of all pregnancies that cause the most detrimental effects to the mother and baby<sup>(2)</sup>. In developing countries they rank next to anemia and accounts for 40000 maternal death annually thereby contributing significantly to maternal and perinatal morbidity and mortality<sup>(3)</sup>.

Preeclampsia is an idiopathic multisystem disorder complicating 6-8% of all pregnancies<sup>(4)</sup>. The pathophysiology of preeclampsia is the development of abnormal placental vasculature early in pregnancy resulting in decreased relative placental perfusion, hypoxemia, ischemia in turn leading to release of antiangiogenic factors into the maternal circulation altering the endothelial functions resulting in hypertension and other manifestations.<sup>(5)</sup>

Magnesium is the second most prevalent intracellular cation of which 60% is complexed with calcium in bone.<sup>(7)</sup> Magnesium acts as a cofactor for many enzymes, is a peripheral vasodilator and improves glucose tolerance. It has significant effects on cardiac excitability and vascular tone, contractility and reactivity. It is a membrane stabilizer.<sup>(1,8)</sup>

#### **HYPOTHESIS:**

Based on the study following hypothesis is formulated

H1. There is a significant association between dietary factors of low level of Magnesium and development of pre-eclampsia and eclampsia.

#### **OBJECTIVE:**

To find out the association between dietary factor of low magnesium and development of pre-eclampsia and eclampsia.

### **II. REVIEW OF LITERATURE**

Shilpa Mittal et Al (2014) conducted a study on Comparison of serum calcium and magnesium levels between preeclamptic and normotensive healthy pregnant women. Study consisted of 100 preeclamptic women in group 1 and group 2 included 100 age matched healthy pregnant women. Results showed serum levels of calcium (8.27+/- 0.37 mg/dl Vs 9.06+/- 0.27 mg/dL) and magnesium (1.99+/-mEq/L Vs 2.03+/-0.13mEq/L) were significantly lower in preeclamptic women than the control group. Study found that hypocalcaemia and hypomagnesemia are seen in the preeclamptic women may be responsible for the vascular pathology associated with onset of preeclampsia. Hence concluded that adjuvant supplementation of calcium and magnesium may prevent further progression of preeclampsia.

Anjum K Saturday, Alka N Sonttake (2013) conducted a cross sectional study on Electrolyte status in preeclampsia. Study subject comprised of three groups aged between 18-35 years. Group 1 - preeclampsia women, group 2- normal pregnant women, group 3- normal healthy controls. Serum was analysed for estimation of calcium, magnesium, sodium and potassium. Results showed reduced levels of serum calcium (7.4+/-0.55mg/dl; 8.68+/- 2.5 mg/dl; 9.61+/-0.95mg/dl), serum magnesium (1.28+/- 1.08; 1.80+/-0.47; 2.31+/-0.35mg/dl), serum potassium (3.37+/-0.25; 3.54+/-0.18; 3.77+/- 0.32 mmol/L) and increased level of sodium (144.9+/- 2.8; 138.2+/- 3.11; 132.6+/-4.4mmol/L) in patients of preeclampsia as compared to normal pregnant women and normal healthy controls respectively. Hence concluded that adjuvant supplementation of calcium, magnesium and potassium with the dietary restriction of sodium may prevent further progression of preeclampsia

Idogun E.S, Imarengiaye C.O, Momoh S.M (2007) conducted a cross sectional study on Extracellular calcium and magnesium in preeclampsia and eclampsia. The study included 11 patients and 23 controls. Result showed plasma calcium was significantly lower in patients than controls (9.2+/-1.02 vs 9.98+/-0.87mg/dl, p 0.043) "t" test. The CSF calcium and magnesium levels were lower in patients than controls (5.66+/-1.22 Vs 6.67+/- 1.15mg/dl, p0.043 and 1.75+/- 0.56 Vs 1.91+/-0.19mg/dl, p<0.0001) respectively. Study concluded that there is a Extracellular calcium and magnesium reduction in patients with preeclampsia and eclampsia. Thus reduction may have a cause and effect relationship with these disorders. Zohreh Taviana, Sara Hossenmirzaei (2013) conducted a cross sectional study on Comparison of maternal serum magnesium level in preeclampsia and normal pregnant women. Study enrolled 50 pregnant women with gestational age of 18-22 weeks, 26 cases with diagnosis of preeclampsia were detected at the next referral. For each cases, 2 normal pregnant women, at the same gestational age, were considered as the control group. Results showed the initial level of magnesium in preeclampsia women was not only significantly less than the control group (1.81+/-0.25mg/dl Vs 2.3+/- 0.44mg/dl, p <0.001) but also the secondary level was low, when the diagnosis was confirmed (1.72+/-0.38mg/dl Vs 2.2+/-0.63mg/dl, p<0.05). Thus the study concluded that checking the levels of magnesium should be considered as the predicting factor of preeclampsia during the first evaluation of pregnancy.

Jagannath Pairu, Triveni G S, Ankitha Manohar (2015) conducted a comparative study of serum calcium and magnesium in pregnancy induced hypertension and normal pregnancy. Study was undertaken in 100 pregnant women. Data for the study was collected from 50 normotensive pregnant women with more than 20 weeks of gestational age (control group) and 50 PIH patients (study group). Results showed that the mean serum calcium is significantly lower in PIH group (8.15+/-0.37mg/dl) compared to normal pregnancy (9.16+/-0.82mg/dl). The mean serum magnesium is lower in PIH group (1.78+/-0.7mEq/L) than normal pregnancy (2.08+/-0.46mEq/L) which is moderately significant. The study concluded that the serum calcium and magnesium levels are decreased in PIH patients compared to normotensive normal pregnant women, suggesting the possible role of calcium and magnesium in etiopathophysiology of pregnancy induced hypertension.

Richard Kobina Dadzie Ephraim et Al (2014) conducted a case control study on serum calcium and magnesium levels in women presenting with preeclampsia and pregnancy induced hypertension in the Cape Coast Metropolis, Ghana. This was conducted on 380 pregnant women of which 120 women were pregnancy induced hypertension, 100 women with preeclampsia and 160 healthy, age matched pregnant women (controls). Results showed systolic blood pressure (155.17±10.21) and diastolic blood pressure (101.63±7.84) were significantly raised in women with pregnancy induced hypertension ( $p < 0.0001$ ) and preeclampsia ( $p < 0.0001$ ). Women with hypertensive disorders (preeclampsia and PIH) had significantly lower serum calcium ( $< 2.1 \text{ mmol/L}$ ) and serum magnesium ( $< 1.5 \text{ mmol/L}$ ) levels than those in the control group (calcium : 2.1-2.8 mmol/L and magnesium 1.5-2 mmol/L) with  $p < 0.0001$ /each. Of those with PIH, SBP correlated positively with the BMI ( $r = 0.575, p < 0.01$ ) and calcium correlated positively with magnesium ( $r = 0.494, p < 0.01$ ). Multivariate analysis showed that women aged  $\geq 40$  years were at a significant risk of developing PIH ( $r = 2.14, p = 0.000$ ). Study concluded that serum calcium and magnesium levels are lower in PIH and preeclampsia than in normal pregnancy. Mineral supplementation during the antenatal period may influence significantly the occurrence of hypertensive disorders of pregnancy.

Abiodun Olusanya, Adekunle O Oguntayo, Aliyu I Sambo (2015) conducted a study on serum levels of calcium and magnesium in preeclamptic- eclamptic patients in a tertiary institution. Study consisted of 48 patients with preeclampsia, 30 patients with eclampsia, and 78 normal pregnant women. All the were either in third trimester or within the puerperium. Results showed that the serum calcium in the preeclamptic and eclamptic patients were significantly lower than in normal pregnant women ( $2.05 \pm 0.4 \text{ mmol/L}$ ,  $1.9 \pm 0.2 \text{ mmol/L}$  Vs  $2.6 \pm 0.4 \text{ mmol/L}$ ,  $p < 0.000$ ). Unlike serum calcium, serum magnesium was lower in the patients with either preeclampsia or eclampsia compared with normal pregnant women but the difference was not statistically significant. This study revealed that serum calcium and magnesium in preeclampsia/eclampsia are lowered compared to normal pregnancy. It was also revealed in this study that serum calcium and magnesium are lower in patients with eclampsia compared to patients with preeclampsia. These findings support the hypothesis that hypocalcaemia and hypomagnesemia may play a role in the pathogenesis of preeclampsia- eclampsia.

Heiner C. Butcher et al ( 1996) conducted a study on Effect of calcium supplementation on pregnancy induced hypertension and preeclampsia. A meta-analysis of randomised controlled trials. Data source was from MEDLINE and EMBASE for 1966 to May 1994. Study selection included fourteen randomised trials involving 2459 women were eligible. The pooled analysis showed a reduction in systolic blood pressure of  $-5.40 \text{ mmHg}$  (95% confidence interval,  $-7.81$  to  $-3.00 \text{ mmHg}$ ;  $p < 0.001$ ) and in diastolic blood pressure of  $-3.44 \text{ mmHg}$  (95% CI,  $-5.20$  to  $-1.68 \text{ mmHg}$ ;  $p < 0.001$ ). The odds ratio for preeclampsia in women with calcium supplementation compared with placebo was 0.38 (95% CI, 0.22 to 0.65). The study concluded that the calcium supplementation during pregnancy leads to an important reduction in systolic and diastolic blood pressure and preeclampsia. While pregnant women at risk of preeclampsia should consider taking calcium, many more patient events are needed to confirm calcium's impact on maternal and fetal morbidity.

### III. DISCUSSION

This is a comparative prospective study consisting of 300 pregnant women with Low level of Serum Magnesium (cases) and 300 women with Normal level of Serum Magnesium (controls), done to study the association between dietary factor of low magnesium and development of pre-eclampsia and eclampsia.

**Table 1: Frequency distribution of BMI**

Normal level of Serum $\text{Mg}^{2+}$ Cases		Cases with Low Serum $\text{Mg}^{2+}$ levels	
BMI	Frequency	BMI	Frequency
12-15'	0	12-15'	0
15-18'	32	15-18'	0
18-21'	87	18-21'	0
21-24'	49	21-24'	132
24-27'	74	24-27'	108
27-30'	24	27-30'	36
30-33'	34	30-33'	24
Total	300		300

**Table 2: Relative frequency of BMI**

Normal level of Serum Mg <sup>2+</sup> Cases			Cases with Low Serum Mg <sup>2+</sup> levels		
BMI	Frequency	Relave Frequency	BMI	Frequency	Relave Frequency
12-15'	0	0	12-15'	0	0
15-18'	32	0.11	15-18'	0	0
18-21'	87	0.29	18-21'	0	0
21-24'	49	0.16	21-24'	132	0.44
24-27'	74	0.25	24-27'	108	0.36
27-30'	24	0.08	27-30'	36	0.12
30-33'	34	0.11	30-33'	24	0.08
Total	300	1		300	1

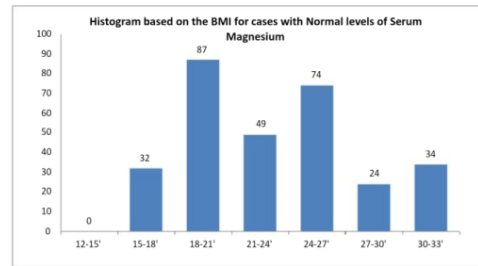


Figure 1

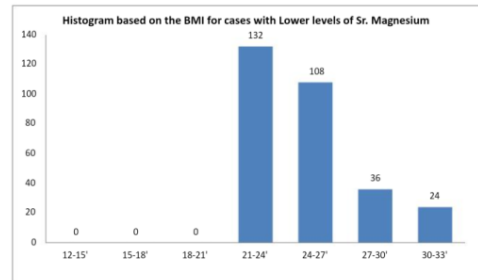


Figure 2

From the Table 1, 2 and Figure 1,2 Individuals having Normal levels of Serum Magnesium tend to have their corresponding BMI in between 18-21 and 24-27, whereas Individuals having Lower levels of Serum Magnesium tend to have their corresponding BMI between 21-24 and 24-27.

**Table 3: Frequency Distribution of Systolic Blood Pressure**

Systolic BP, Normal Cases		Systolic BP, Cases with Low Serum Mg <sup>2+</sup> levels	
Bins	Frequency	Bins	Frequency
70-80'	10	70-80'	0
80-90'	33	80-90'	0
90-100'	49	90-100'	0
100-110'	87	100-110'	0
110-120'	67	110-120'	95
120-130'	47	120-130'	119
130-140'	1	130-140'	60
140 and more	6	140 and more	26
Total	300	Total	300

**Table 4: Frequency Distribution of Diastolic Blood Pressure**

Diastolic BP, Normal Case		Diastolic BP, Cases with Low Serum Mg <sup>2+</sup> levels	
Bins	Frequency	Bins	Frequency
40-50'	21	40-50'	0
50-60'	55	50-60'	0
60-70'	150	60-70'	0
70-80'	44	70-80'	82
80-90'	22	80-90'	132
90 and more	8	90 and more	86
	300		300

**Table 5: Blood Pressure analysis of Normal Level of Serum Magnesium Cases**

Normal Cases	Mean	Median	Maximum	Minimum	Std. Dev
Systole	101.6266667	100	190	70	16.051567
Diastole	60.50666667	60	114	40	11.61175

**Table 6: Blood Pressure analysis of Low Level of Serum Magnesium Cases**

Cases with Low Mg <sup>2+</sup> levels	Mean	Median	Maximum	Minimum	Std. Dev
Systole	121.16	120	190	104	16.487182
Diastole	79.36	80	120	62	10.358962

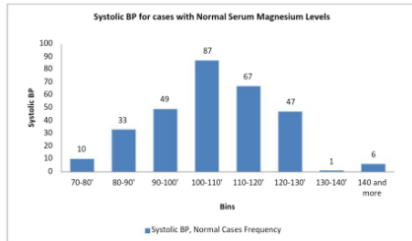


Figure 3

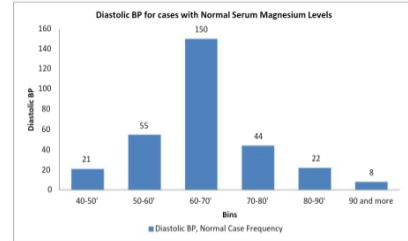


Figure 5

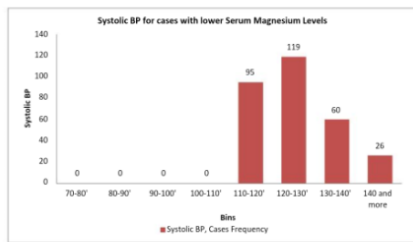


Figure 4

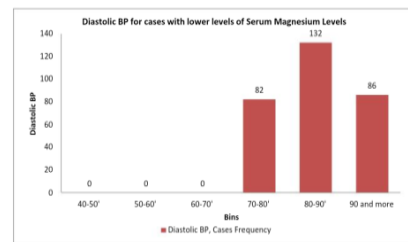


Figure 6

From the analysis of the above tables 3 to 6 and Figures 3 to 6, it is evident that individuals with lower serum magnesium levels tend to have a high systolic BP of 140 or above and a diastolic BP of 90 or above. This is one of the key features in the development of Pre-Eclampsia and Eclampsia. Furthermore this discrepancy was further validated with a p-value of 0.0031 for the systolic BP and a p-value of 0.0047 for the Diastolic BP.

**Table 7: Frequency distribution of Proteinuria for normal level of serum magnesium cases**

Cases with Normal Serum Magnesium Levels	Systolic BP < 140	Systolic BP > 140
Proteinuria < 3 grams/Day	294	0
Proteinuria > 3 grams /Day	0	6

Cases with Normal Serum Magnesium Levels	Diastolic BP < 90	Diastolic BP > 90
Proteinuria < 3 grams/Day	292	0
Proteinuria > 3 grams /Day	0	8

**Table 8: Frequency distribution of Proteinuria for Low level of serum magnesium cases**

Cases with Low Serum Magnesium Levels	Systolic BP < 140	Systolic BP > 140
Proteinuria < 3 grams/Day	274	0
Proteinuria > 3 grams /Day	0	26

Cases with Low Serum Magnesium Levels	Diastolic BP < 90	Diastolic BP > 90
Proteinuria < 3 grams/Day	271	0
Proteinuria > 3 grams /Day	0	29

From Table 7 and 8, it is clear that individuals with lower serum magnesium levels having pre-eclampsia and eclampsia have a significant amount of proteinuria, i.e. 3gm/day or more.

**Table 9: Descriptive Analysis of Serum Magnesium**

Cases with Normal Serum Mg <sup>2+</sup> levels		Cases with Low Serum Mg <sup>2+</sup> Levels	
Parameters	Values	Parameters	Values
Mean	1.921866667	Mean	1.137333333
Standard Error	0.018640217	Standard Error	0.016220975
Median	1.9	Median	1.2
Mode	1.9	Mode	1.2
Standard Deviaon	0.322858029	Standard Deviaon	0.280955528
Sample Variance	0.104237307	Sample Variance	0.078936009
Kurtosis	6.775548591	Kurtosis	1.694414551
Skewness	2.039746662	Skewness	0.891316001
Range	1.73	Range	1.4
Minimum	0.67	Minimum	0.6
Maximum	2.4	Maximum	2
Sum	576.56	Sum	341.2
Count	300	Count	300
Condence Level(95.0%)	0.036682635	Condence Level(95.0%)	0.031921737

**Table 10: Frequency distribution of Serum Magnesium**

Frequency Distribuon, Normal Serum Mg <sup>2+</sup>		Frequency Distribuon, Lower Serum Mg <sup>2+</sup>	
Bin	Frequency	Bin	Frequency
0.5'	0	0.5'	0
0.5-1'	0	0.5-1'	135
1-1.5'	0	1-1.5'	165
1.5-2'	194	1.5-2'	0
2-2.5'	106	2-2.5'	0
Total	300	Total	300

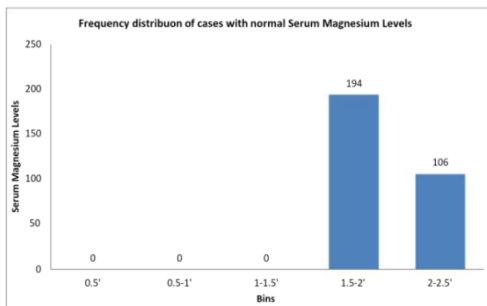


Figure 7

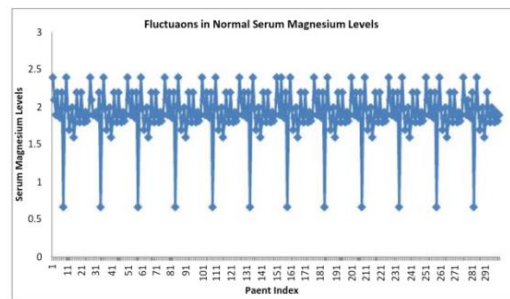


Figure 9

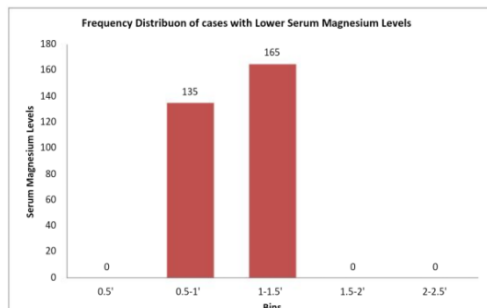


Figure 8

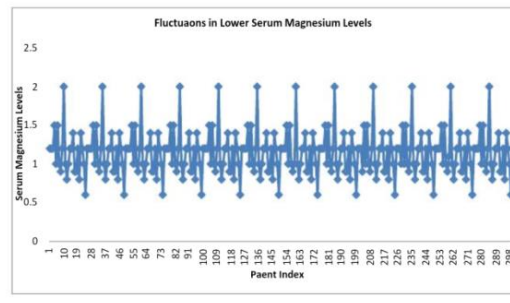


Figure 10

From the descriptive analysis carried out from the tables 9, 10 and figures 7 to 10, it is clear that the Serum Magnesium levels are lower in the pre-eclampsia and eclampsia cases when compared with the normal cases. It is clear that the Serum Magnesium levels are lower and vary in an erratic fashion in low serum magnesium cases than in the normal serum magnesium cases.

#### IV. CONCLUSION

Hypertensive disorders of pregnancy is one of the major causes of maternal and fetal morbidity and mortality. It forms a member of the deadly triad, along with hemorrhage and infection. Yet as long as its etiopathogenesis is unclear, prophylaxis will be uncertain. Though the prevention is difficult, maternal and fetal morbidity and mortality can be reduced to a greater extent by early recognition and timely management.

Pregnancy is associated with physiological decrease in the concentration of elements like calcium and magnesium which is further aggravated in conditions like preeclampsia. As the severity of preeclampsia increases, more and more reduction in the levels of magnesium is seen in maternal blood.

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